

# Type 1 Diabetes in Children: Chronic Complications and their Clinical Impact

*Xasanova Nargis Qodirovna*

*Department of Fundamental Medical Sciences of the Asian International University, Bukhara, Uzbekistan*

**Abstract:** Type 1 diabetes mellitus (T1DM) is one of the most common chronic endocrine disorders in childhood. Although advances in insulin therapy and glucose monitoring have improved outcomes, children remain at risk of both acute and long-term complications. This study aims to highlight the major complications of T1DM in pediatric patients and evaluate their clinical consequences. Acute complications such as diabetic ketoacidosis (DKA) and severe hypoglycemia are frequent and life-threatening. Chronic complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease, may begin early in life and significantly affect morbidity and quality of life. Early recognition and prevention strategies are essential to reduce the burden of these complications.

**Keywords:** Type 1 diabetes, microvascular complications, macrovascular complications, retinopathy, nephropathy, neuropathy.

Type 1 diabetes (T1DM) is an autoimmune disease characterized by hyperglycemia secondary to pancreatic beta cell destruction leading to insufficient insulin production. Maintaining normal blood sugar and avoiding hypoglycemia or hyperglycemia is achieved by administering the treatment (insulin) after evaluating all factors (type of insulin, blood sugar level, other associated chronic or acute diseases, stress, and hormonal imbalances). These steps are difficult to achieve and maintain in the absence of adequate medical education. Education targets both the patient and their family. Despite the availability of modern insulin regimens, continuous glucose monitoring, and improved patient education, pediatric patients are still highly vulnerable to complications.

Complications of T1DM can be broadly classified into:

- **Acute complications**, such as diabetic ketoacidosis (DKA) and hypoglycemia.
- **Chronic complications**, including microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (hypertension, dyslipidemia, early atherosclerosis) manifestations.

Understanding the frequency and clinical consequences of these complications in children is critical for optimizing management and preventing long-term morbidity. The aim of this paper is to review the complications of T1DM in children and discuss their clinical impact.

Chronic complications, including diabetic retinopathy, nephropathy, neuropathy, and early cardiovascular disease, can begin during childhood and adolescence, especially in cases of poor glycemic control. These complications contribute to morbidity, reduced quality of life, and increased healthcare burden. This paper aims to review the prevalence, mechanisms, and clinical impact of chronic complications of T1DM in pediatric patients, emphasizing the importance of early detection and prevention strategies.

## Classification of Chronic Complications of Type 1 Diabetes in Children

Chronic complications of type 1 diabetes mellitus (T1DM) can be broadly classified into microvascular, macrovascular, and other systemic complications:

### 1. Microvascular Complications

- Eye disease

- ✓ Diabetic retinopathy (nonproliferative, proliferative)
- ✓ Diabetic macular edema
- ✓ Cataracts
- ✓ Glaucoma
- Neuropathy
- ✓ Peripheral neuropathy (sensory and motor; mono- and polyneuropathy)
- ✓ Autonomic neuropathy (cardiovascular, gastrointestinal, genitourinary, sudomotor dysfunction)
- Nephropathy
- ✓ Persistent albuminuria
- ✓ Declining renal function leading to chronic kidney disease

## 2. Macrovascular Complications

- ✓ Coronary heart disease (CHD)
- ✓ Peripheral arterial disease (PAD)
- ✓ Cerebrovascular disease (stroke, transient ischemic attack)
- ✓ Heart failure

## 3. Other Complications

- ✓ Gastrointestinal: diabetic gastroparesis, chronic diarrhea
- ✓ Genitourinary: bladder dysfunction, sexual dysfunction
- ✓ Dermatologic: diabetic dermopathy, necrobiosis lipoidica, poor wound healing
- ✓ Infectious complications: increased susceptibility to bacterial and fungal infections
- ✓ Musculoskeletal: limited joint mobility (diabetic cheiroarthropathy)
- ✓ Oral complications: periodontal disease
- ✓ Sensory complications: hearing loss

## Mechanisms of complications

Chronic hyperglycemia is the important etiologic factor leading to complications of DM, but the mechanism(s) by which it leads to such diverse cellular and organ dysfunction is unknown. The complications are likely multifactorial with an emerging hypothesis that hyperglycemia leads to epigenetic changes (Chap. 479) that influence gene expression in affected cells. Chronic hyperglycemia leads to formation of advanced glycosylation end products (AGEs; e.g., pentosidine, glu cosepane, and carboxymethyllysine), which bind to specific cell surface receptor and/or the nonenzymatic glycosylation of intra- and extracellular proteins, leading to cross-linking of proteins, glomerular dysfunction, endothelial dysfunction, altered extracellular matrix composition, and accelerated atherosclerosis. Growth factors may play an important role in some diabetes related microvascular complications. For example, vascular endothelial growth factor A (VEGF-A) is increased locally in diabetic proliferative retinopathy, decreases after laser photocoagulation, and is the target inhibited by intravitreal injection therapy. A possible unifying mechanism is that hyperglycemia leads to increased production of reactive oxygen species or superoxide in the mitochondria and this may activate several pathways. Although hyperglycemia serves as the initial trigger for complications of diabetes, it is still unknown whether the same pathophysiologic processes are operative in all complications or whether some pathways predominate in certain organs. The mechanisms of diabetes-related macrovascular complications including MI and stroke also include traditional cardiovascular risk factors (dyslipidemia, hypertension), insulin resistance, and inflamma

tion. In T2DM, insulin resistance is present years prior to diagnosis and is associated with obesity and ectopic accumulation of lipids and fat in liver and muscle. Additionally, insulin fails to appropriately suppress lipolysis from adipose tissue, which results in increased delivery of fatty acids to liver, muscle, endothelial cells, and cardiac tissues, leading to tissue accumulation of triglycerides, diacylglycerol, and ceramides.

### **Ophthalmologic complications of diabetes mellitus**

Diabetic retinopathy is a microvascular complication of type 1 diabetes characterized by progressive damage to the retinal blood vessels, leading to increased vascular permeability, microaneurysms, hemorrhages, and in advanced stages, neovascularization. It represents a major cause of vision impairment and blindness in children and adolescents with long-standing diabetes, particularly in those with poor glycemic control. Diabetic retinopathy is classified into two stages: nonproliferative and proliferative. Nonproliferative diabetic retinopathy usually appears late in the first decade or early in the second decade of hyperglycemia and is marked by retinal vascular microaneurysms, blot hemorrhages, and cotton-wool spots. Mild nonproliferative retinopathy may progress to more extensive disease, characterized by changes in venous vessel caliber, intraretinal microvascular abnormalities, and more numerous microaneurysms and hemorrhages. The pathophysiologic mechanisms invoked in nonproliferative retinopathy include loss of retinal pericytes, increased retinal vascular permeability, alterations in retinal blood flow, and abnormal retinal microvasculature, all of which can lead to retinal ischemia. The appearance of neovascularization in response to retinal hypoxemia is the hallmark of proliferative diabetic retinopathy. These newly formed vessels appear near the optic nerve and/or macula and rupture easily, leading to vitreous hemorrhage, fibrosis, and ultimately retinal detachment.

### **Renal complications of diabetes mellitus**

Diabetic nephropathy is a chronic microvascular complication of type 1 diabetes characterized by structural and functional damage to the kidneys, initially presenting as persistent microalbuminuria and later progressing to proteinuria, declining glomerular filtration rate, and chronic kidney disease. It is a leading cause of end-stage renal failure and significantly contributes to morbidity and mortality in diabetic patients. Like other microvascular complications, the pathogenesis of diabetic nephropathy is related to chronic hyperglycemia. The mechanisms by which chronic hyperglycemia leads to diabetic nephropathy are incompletely defined but involve the effects of soluble factors (growth factors, angiotensin II, endothelin, AGEs), epigenetic changes, hemodynamic alterations in the renal microcirculation (glomerular hyperfiltration or hyperperfusion, increased glomerular capillary pressure), structural changes in the glomerulus (increased extracellular matrix, basement membrane thickening, mesangial expansion, fibrosis), and tubular dysfunction (tubulointerstitial damage, fibrosis). The natural history of diabetic nephropathy is characterized by a sequence of events that was initially defined for individuals with type 1 DM but appears similar in type 2 DM. Glomerular hyperperfusion and renal hypertrophy occur in the first years after the onset of DM and are associated with an increase of the estimated glomerular filtration rate (GFR). During the first 5 years of DM, thickening of the glomerular basement membrane, glomerular hypertrophy, and mesangial volume expansion occur as the GFR returns to normal. Once there is marked albuminuria and a reduction in GFR, these pathologic changes are likely irreversible. As part of comprehensive diabetes care, diabetic nephropathy should be detected at an early stage when effective therapies can be instituted.

### **Neuropathy and diabetes mellitus**

Diabetic neuropathy is a common chronic microvascular complication of type 1 diabetes resulting from long-standing hyperglycemia and metabolic imbalance, leading to progressive damage of peripheral and autonomic nerves. It manifests as sensory and motor dysfunction, such as distal symmetric polyneuropathy, mononeuropathies, and autonomic neuropathy, which can significantly impair quality of life and increase the risk of morbidity in pediatric and adolescent patients. Diabetic neuropathy, which occurs in ~50% of individuals with long standing type 1, manifests as a diffuse neuropathy (distal symmetrical polyneuropathy and/or autonomic neuropathy), a mononeuropathy,

and/or a radiculopathy/polyradiculopathy. As with other complications of DM, the development of neuropathy correlates with the duration of diabetes and glycemic control. Additional risk factors are body mass index (BMI) (the greater the BMI, the greater the risk of neuropathy) and smoking. The presence of ASCVD, elevated triglycerides, and hypertension is also associated with diabetic peripheral neuropathy. Both myelinated and unmyelinated nerve fibers are lost. Because the clinical features of diabetic neuropathy are similar to those of other neuropathies, the diagnosis of diabetic neuropathy should be made only after other possible etiologies are excluded.

## Conclusion

Type 1 diabetes mellitus in children is a chronic autoimmune condition that, despite advances in insulin therapy and modern glucose monitoring systems, continues to predispose patients to serious long-term complications. Chronic hyperglycemia remains the key driver of microvascular and macrovascular damage, mediated through complex mechanisms including advanced glycation end products, oxidative stress, endothelial dysfunction, and growth factor activation.

Among microvascular complications, **diabetic retinopathy, nephropathy, and neuropathy** represent the most prevalent and clinically significant conditions, with early manifestations beginning in childhood or adolescence. These complications can lead to irreversible organ damage, reduced quality of life, and increased risk of disability. Macrovascular complications, although more common in adults, may also develop early, with evidence of subclinical atherosclerosis in pediatric patients. Additional systemic complications—such as gastrointestinal, dermatologic, genitourinary, and musculoskeletal disorders—further increase the disease burden.

Early recognition and timely intervention remain the cornerstone of reducing morbidity and mortality associated with T1DM. Regular screening, optimization of glycemic control, patient and family education, and a multidisciplinary approach are essential strategies to prevent or delay the onset of complications. Strengthening awareness of chronic complications in pediatric populations is critical to improving long-term outcomes and ensuring a better quality of life for children living with type 1 diabetes.

## Used literature :

1. Chiang JL, Maahs DM, Garvey KC, Hood KK, Laffel LM, Weinzimer SA, Wolfsdorf JI, Schatz D. Type 1 Diabetes in Children and Adolescents: A Position Statement by the American Diabetes Association. *Diabetes Care*. 2018 Sep;41(9):2026-2044.
2. American Diabetes Association. 13. Children and Adolescents: *Standards of Medical Care in Diabetes-2019*. *Diabetes Care*. 2019 Jan;42(Suppl 1):S148-S164
3. Insel RA, Dunne JL, Atkinson MA, Chiang JL, Dabelea D, Gottlieb PA, Greenbaum CJ, Herold KC, Krischer JP, Lernmark Å, Ratner RE, Rewers MJ, Schatz DA, Skyler JS, Sosenko JM, Ziegler AG. Staging presymptomatic type 1 diabetes: a scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. *Diabetes Care*. 2015 Oct;38(10):1964-74.
4. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. *Lancet*. 2014 Jan 04;383(9911):69-82.
5. Triolo TM, Fouts A, Pyle L, Yu L, Gottlieb PA, Steck AK., Type 1 Diabetes TrialNet Study Group. Identical and Nonidentical Twins: Risk and Factors Involved in Development of Islet Autoimmunity and Type 1 Diabetes. *Diabetes Care*. 2019 Feb;42(2):192-199.
6. Wolfsdorf JI, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, Sperling MA, Codner E. ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *Pediatr Diabetes*. 2018 Oct;19 Suppl 27:155-177.
7. Hanas R. Type 1 Diabetes in Children, Adolescents and Young Adults (How to become an expert on your own diabetes). Preface to eighth edition, pages XII, Class Publishing Ltd., London, 2022.

8. Phelan H, King B, Anderson D, Crock P, Lopez P, Smart C. Young children with type 1 diabetes can achieve glycemic targets without hypoglycemia: Results of a novel intensive diabetes management program. *Pediatr Diabetes*. 2018;19:769-775.
9. Sundberg F, deBeaufort C, Krogvold L, Patton S, Piloya T, Smart C, Van Name M, Weissberg-Benchell J, Silva J, diMeglio LA. ISPAD Clinical Practice Consensus Guidelines 2022: Managing diabetes in preschoolers. *Pediatr Diabetes*. 2022;23:1496-1511.
10. Annan SF, Higgins LA, Jelleryd E, Hannon T, Rose S, Salis S, Baptista J, Chinchilla P, Marcovecchio ML. ISPAD Clinical Practice Consensus Guidelines 2022: Nutritional management in children and adolescents with diabetes. *Pediatr Diabetes*. 2022;23:1297-1321. Epub 2022 Dec 5